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General Status of Cytokines in Acute Obstructive Bronchitis in Frequently ILL Children

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Abstract: Acute obstructive bronchitis remains one of the most prevalent and severe respiratory diseases in children. Understanding the pathogenetic role of immune status and cytokines can provide deeper insight into the mechanisms underlying the development of AOB. This knowledge is essential for developing effective diagnostic and treatment strategies for frequently ill children.

The primary focus of scientific research is to investigate the mechanisms of disease progression, identify the clinical features, and assess the impact of immune status and cytokines in acute obstructive bronchitis among frequently ill children. The goal is to develop pathogenetically based treatment methods and preventive measures.

In our country, extensive efforts are being made to ensure early diagnosis and prevention of somatic diseases in children, with particular emphasis on bronchopulmonary pathology.

Keywords: obstructive bronchitis, cytokines, immunity, frequently ill children.

Relevance. In pediatric practice, one of the key modern diagnostic markers for identifying "frequently ill children" is the assessment of local and systemic immune parameters, as well as inflammatory and anti-inflammatory cytokines. However, their role in the development of pathological processes is primarily considered from the perspective of their interactions. It is well established that recurrent respiratory illnesses in children, including acute obstructive bronchitis, disrupt compensatory-adaptive mechanisms, leading to chronic recurrent infections and impairments in both cellular and humoral immunity [1,3,8].

In children, viral infections often result in a weakened respiratory defense system, allowing viruses to persist and replicate in the epithelium. In allergic reactions affecting the respiratory mucosa, inflammatory metabolites trigger the release of inflammatory mediators. Meanwhile, immune system alterations contribute to the formation of cytotoxic antibodies within the bronchial submucosa, ultimately leading to obstructive syndrome [6,9]. Several researchers highlight the significance of cytokine profiling in patients with obstructive bronchitis, as an imbalance in cytokine levels is a key driver of inflammation in the respiratory tract [2,4]. The investigation of cytokines' role in disease pathogenesis remains highly relevant today [7,11].

Cytokines are glycosylated polypeptides that regulate immune responses. Based on their biological activity, they are classified into regulators of humoral and cellular immunity, mediators of allergic reactions, or modulators of immunosuppressive responses [5,12]. Their role in controlling inflammation is crucial in the pathogenesis of obstructive bronchitis [10].

Objective of the Study. To examine the cytokine profile in children with acute obstructive bronchitis who experience frequent illness.

Materials and Methods. To assess correlations with cytokine profile indicators, a study was conducted involving 120 patients diagnosed with acute obstructive bronchitis. The participants were divided into two groups:Group I – 40 patients with acute obstructive bronchitis classified as "episodically ill children. "Group II – 80 patients with acute obstructive bronchitis belonging to the "frequently ill children" category.

Research Findings. Interleukins play a crucial role in various biological processes, including the activation, differentiation, and proliferation of immune cells, as well as in the regulation of innate and adaptive immune responses and inflammation.

The study of cytokine levels revealed significant differences in nearly all examined parameters between patients in Table 1.

Cytokine parameters in patients with Acute obstructive bronchitisduring hospitalization (M±m).

Indicators	The norm	Group I	Group II	P_1	P_2	P_3
IL-1β, pg/ml	6,23±0,32	29,85±1,00	22,25±0,42	<0,001	<0,001	<0,001
IL-4, pg/ml	4,85±0,32	12,60±0,24	9,60±0,18	<0,001	<0,001	<0,001
IL-6, pg/ml	17,27±0,73	19,62±0,54	22,95±0,39	<0,01	<0,01	<0,001
IL-8, pg/ml	10,34±0,37	19,85±0,73	23,25±0,40	<0,001	<0,001	<0,001
IL-10, pg/ml	10,34±0,57	22,80±0,57	33,12±0,70	<0,001	<0,001	<0,001
TNF-α, pg/ml	24,81±1,03	28,58±1,08	32,16±0,70	<0,001	<0,01	<0,01

Note:P1 – Standard values vs. children with acute obstructive bronchitis

P2 – Normal values vs. children with acute obstructive bronchitis

P3 – Significance of differences between children with acute obstructive bronchitis from different groups

In children with episodic acute obstructive bronchitis, the production of endogenous pro-inflammatory IL-1 increased 4.8 times, IL-4 by 2.6 times, IL-10 by 2.2 times, while anti-inflammatory cytokines IL-6 rose by 1.1 times, IL-8 by 1.9 times, and TNF-α by 1.2 times compared to normal levels ($P<0.01$, $P<0.001$).

The rise in cytokine levels results from the impact of infectious agents that trigger acute obstructive bronchitis. Their equilibrium plays a crucial role in determining the disease progression and prognosis.

The elevated IL-1 levels in Group I, considering its involvement in inflammatory responses, contribute to airway swelling and narrowing, a hallmark of obstructive bronchitis in children. IL-4, primarily secreted by T-lymphocytes and basophils, promotes IgE synthesis, thereby intensifying allergic reactions in the bronchi during acute obstructive bronchitis.

In children with episodic disease, the moderate elevation of IL-6 in the bloodstream confirms the presence of inflammatory and infectious processes in the respiratory tract. However, excessive IL-6 levels may amplify the inflammatory response and worsen disease symptoms. The IL-8 concentration in episodic acute obstructive bronchitis patients increased to 19.85 ± 0.73 pg/ml, reflecting an inflammatory reaction in the respiratory tract. This activates neutrophils, which play a critical role in immune defense and indicate a dominance of cellular immunity over humoral immunity. However, excessive neutrophil activation may exacerbate pathological inflammation, leading to lung tissue damage.

An increased IL-10 level in children with acute obstructive bronchitis may suggest the body's attempt to regulate and mitigate inflammation. Additionally, the elevated TNF-α levels in acute obstructive bronchitis serve as an essential component of the innate immune response. In reaction to infection, TNF-α inhibits the proliferation of intracellular pathogens while simultaneously functioning as an immune regulator, signaling the activation of the immune system and the ongoing inflammatory process. [Хаитов, Р.М. Иммунология / Р.М. Хаитов; научное редактирование А.Л. Ковальчук. – Москва: ГЭОТАР – Медиа, 2016. – 496 с.]

In the group of frequently ill children, the progression of acute obstructive bronchitis was accompanied by an increase in cytokine levels in the bloodstream. Compared to standard values, IL-1 levels rose by 3.6 times, IL-4 by 2 times, IL-6 by 1.3 times, IL-8 by 2.2 times, IL-10 by 3.2 times, and TNF-α by 1.3 times ($P<0.01$, $P<0.001$). However, in comparison with children experiencing episodic acute obstructive bronchitis, IL-1 was 0.7 times lower, IL-4 was reduced by 0.8 times, IL-6 and IL-8 by 1.2 times, IL-10 by 1.5 times, and TNF-α by 1.1 times ($R<0.01$, $R<0.001$). This imbalance serves as a hallmark of pulmonary impairment in this group, emphasizing a distinct immune response pattern in frequently ill children.

IL-1, a key regulator of inflammation and immunity, plays a pivotal role in the activation of T- and B-lymphocytes. Its elevated concentration (22.25 ± 0.42 pg/ml) in frequently ill children with acute obstructive bronchitis intensifies inflammatory processes in the respiratory tract, contributing to a more severe disease course.

A lower IL-4 level in Group II (9.60 ± 0.18 pg/ml) compared to Group I (12.60 ± 0.24 pg/ml, $P<0.001$) suggests a diminished allergic response in frequently ill children with acute obstructive bronchitis.

The increase in IL-6 levels (22.95 ± 0.39 pg/ml) in this group reflects an intensified immune response, stimulating the synthesis of other inflammatory and anti-inflammatory cytokines, including IL-10 and TNF-α, which play a role in modulating the disease's inflammatory processes.

In acute obstructive bronchitis, IL-8 levels (23.25 ± 0.40 pg/ml) were significantly elevated compared to normal ($P<0.001$) and episodic cases ($P<0.01$). IL-8 functions by recruiting neutrophils to the site of inflammation, forming part of systemic immune reactions. However, excessive neutrophil activation may lead to tissue damage and exacerbate airway obstruction.

An increased IL-10 level (33.12 ± 0.70 pg/ml) in frequently ill children compared to the control group indicates its dual function in immune regulation. While IL-10 has protective anti-inflammatory properties by suppressing pro-inflammatory cytokine production and reducing inflammation, it may also inhibit immune cell activation, potentially prolonging the disease and increasing the risk of complications.

The serum TNF-α concentration (32.16 ± 0.70 pg/ml) was significantly higher in children with acute obstructive bronchitis than in the control group ($P<0.01$). TNF-α is a crucial mediator of early cytokine responses, playing a key role in antiviral defense. Its increased levels suggest its involvement in inflammatory processes and immune activation, contributing to disease pathogenesis.

These findings emphasize the essential role of interleukins in the development of acute obstructive bronchitis in frequently ill children. Their concentrations can serve as biomarkers for disease severity, highlighting the importance of monitoring cytokine fluctuations in this group. Studying these immune markers is crucial for advancing diagnostic and therapeutic strategies for acute obstructive bronchitis.

Elevated levels of both anti-inflammatory (IL-1 increased 4.8 times, IL-4 by 2.6 times, IL-10 by 2.2 times) and pro-inflammatory (IL-6 increased 1.1 times, IL-8 by 1.9 times, and TNF-α by 1.2 times) interleukins were observed compared to normal values ($P<0.01$, $P<0.001$). These findings

underscore the importance of pathogenic mechanisms in bronchial obstruction syndrome and highlight the need to regulate immune responses to control disease progression.

Summary. The research demonstrated that cytokines serve as key mediators in the pathogenesis of the disease, orchestrating immune cell activation and inflammatory responses within the respiratory system. Gaining a deeper understanding of their role in obstructive bronchitis in children can shed light on the underlying disease mechanisms, its clinical progression, and potential strategies for diagnosis and treatment.

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